COVID-19: Origin, Transmission and Clinical Therapies on Coronavirus with Current Update

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ABSTRACT

An acute respiratory disorder, triggered by a novel coronavirus (SARS-CoV-2, previously identified as 2019-nCoV), the 2019 coronavirus disorder (COVID-19) has spread across China and has gained global publicity. The COVID-19 outbreak was formally proclaimed an international public health emergency by the WHO. The appearance of SARS-CoV-2, after the 2002 extreme acute coronavirus respiratory syndrome (SARS-CoV) and 2012 coronavirus respiratory syndrome (MERS-CoV) in the Middle East. The disease is spread through inhalation or interaction with contaminated droplets and the time of incubation ranges from 2 to 14 days. The signs generally include fatigue, cough, sore throat, breathlessness, tiredness, malaise, and others. The novel coronavirus utilizes the same transmitter, angiotensin-converting enzyme 2 (ACE2) as the one used by SARS-CoV, which spreads primarily across the airway. Importantly, there has been increasing evidence of sustained human-to-human transmission, along with many cases exported across the globe. There are few specific antiviral strategies, but several potent antiviral and repurposed drug candidates are under urgent investigation. In this study, we outlined the recent medical advancement of COVID-19’s epidemiology, pathogenesis, and clinical features, and addressed new therapy and technological developments to counter the novel coronavirus outbreak.

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INTRODUCTION

Upon examining respiratory tests, doctors from the PRC Centres for Disease Control (CDC) reported that novel coronavirus triggered pneumonia, then identified as novel coronavirus pneumonia (NCP). The illness was formally called COVID-19 by WHO. The International Committee for Virus Taxonomy (ICTV) has identified coronavirus 2 (SARS-CoV-2) extreme acute respiratory syndrome is rapidly spreading from its sources in the Wuhan Area, China Province of Hubei, to the rest of the world [1]. Approximately 96,000 cases of coronavirus disease (COVID-19) and 3,300 deaths were recorded until 05/03/2020 [2]. India has so far registered 29 incidents. Luckily, children have been barely killed with any fatalities so far. Yet the virus's possible path remains uncertain. This article provides a view of this latest virus from a bird's perspective. Despite the constantly emerging awareness regarding this virus, readers are encouraged to refresh themselves periodically. Coronaviruses become immersed in positive-sense RNA viruses varying around 60 nm to 140 nm in size with spikes like structures on its surface giving it a crown-like appearance under an electron microscope; thus the term coronavirus [3]. Four coronaviruses have been in existence in humans, including HKU1, NL63, 229E which OC43, which usually induce moderate respiratory disorder. If the international community reacts to SARS-CoV-2, humanitarian disaster public health officials begin at a loss to implement effective infection management to deter spread in healthcare environments, detect contagious diseases, provide preventive services, and innovative therapies for chronically sick patients, and monitor connections. In emergencies these routine public safety interventions are especially challenging to carry out. Reduced public safety, hospital, and primary care facilities, for example, pose an obstacle to research. This is a problem in all contexts, compounded in dynamic humanitarian situations, to provide the existing healthcare worker infrastructure with adequate preparation and personal protection equipment, and to maintain a consistent supply chain for this. Frequent movement and minimal contact details may prevent successful tracking of contacts. Furthermore, intractable logistical problems such as overcrowding hinder both the quarantine of those infected and the isolation of those sick. Despite such heightened risks, humanitarian emergencies can be treated as a challenge for national and foreign organizations trying to counter this pandemic.
that is unfolding. The common, regional evidence-based strategies to fight respiratory viruses should be applied to minimize the effects of COVID-19 on crisis-affected communities, states, and agencies. Respiratory hygiene is a highly successful factor in public safety, backed by proof that the transmission of respiratory viruses, such as SARS-CoV-2, may be avoided by hand grooming, good cough exercise, and social distancing [4]. Hand hygiene is a readily applied behaviour: it has been seen that the provision of soap to households in humanitarian settings improves hand washing by more than 30 percent [5].

Origin

In December 2019, adults started pre-sending to local hospitals with serious pneumonia of unclear origin in Wuhan, the capital city of Hubei province, and a big transportation center in China. Many of the original cases had a popular connection to the wholesale Huanan seafood industry, which often exchanged live animals. The surveillance network (set up after the SARS outbreak) was triggered, and patient respiratory samples were sent to reference laboratories for etiological investigations [8]. China reported the epidemic to the World Health Organisation on 31 December 2019 and the Huanan seafood market closed on 1 January. The virus was described on January 7 as a coronavirus with 95% homology to the bat coronavirus and around 70% resemblance to the SARS-CoV. Environmental tests from the seafood market in Huanan have screened positively, suggesting that the virus came from there [7].

Transmission

The number of cases began to rise exponentially, some of which were not exposed to the live animal market, suggesting that human-to-human transmission was taking place [8]. By 23 January, with restrictions on entry and exit from the city, the 11 million Wuhan population was placed under lockdown. The lock-down was quickly expanded to other major cities in Hubei. Cases of COVID-19 in countries outside China have been identified in those with no travel background to China, indicating that there was local human-to-human transmission in those countries [9]. Airports in numerous countries like India placed in screening systems to detect symptom people returning from China and place them in isolation and COVID-19 monitoring. It soon became apparent that the infection could be transmitted from asymptomatic individuals, and also before symptoms began. Countries like India, therefore, which evacuated their residents from Wuhan by special flights or had travellers returning from China, but all people in isolation for 14 days, and screened them for the virus. India, which had only registered 3 cases before 3/3/2020. By 6/3/2020, 29 cases had been reported; in Italian tourists and their contacts mostly in Delhi, Jaipur, Agra, and Mathura. By 13 May 2020, 74952 incidents were recorded with 2436 fatalities. One case was identified by an Indian who flew back from Austria and humiliated a significant number of school children at a city hotel birthday party. Some of the associates in such incidents have been quarantined. Due to shortcomings in monitoring and examination, such figures could be an underestimation of the sick and deceased. Since the SARS-CoV-2 had its roots in bats [10].

Epidemiology

Infection is spread by broad droplets produced by symptomatic patients while coughing and sneezing, but may also occur from asymptomatic patients and before symptoms begin [11]. Studies have reported higher viral loads in the nasal cavity than in the mouth, but no disparity in viral load between symptomatic and asymptomatic individuals [12]. For as long as the effects continue and even during surgical treatment, patients can remain contagious. Some people can behave as super spreaders; a citizen of the United Kingdom who attended a conference in Singapore contaminated 11 others while staying in a resort in the French Alps and returning to Britain [8]. In ideal atmospheric environments, the virus will stay viable on surfaces for days but is killed in less than a minute by specific disinfectants such as sodium hypochlorite, hydrogen peroxide, etc. [13]. Infection is obtained by either inhaling these droplets or contacting infected objects and then rubbing the nose, ears, and eyes. The virus is also present in the stool and water source pollution.

Genome Structure and Key Viral Factors

The full genome of Wuhan-Hu-1 coronavirus (HCV), one strain of SARS-CoV-2, isolated from COVID-19 pneumonia patient, a worker on the Wuhan seafood market, is 29.9 kb [14]. Although SARS-CoV and MERS-CoV have 27.9 kb and 30.1 kb of positivesense RNA genomes, respectively [15]. The CoVs genome has been shown to produce a variable number (6-11) of free read frames (ORFs) [16]. Two-thirds of viral RNA, found primarily in the first ORF (ORF1a/b), translates two polyproteins, pp1a and pp1ab, and codes 16 non-structural proteins (NSP), while the remaining ORFs encode accessory and structural proteins. The remainder of the genome of viruses encodes four basic structural proteins [1].

Coronavirus genetics

Until recently, the genetics of coronavirus replication and pathogenesis is primarily researched using natural mutations, mutants of the host family, transferred viruses, and mutagenized viruses were chosen for temperature sensitiveness and precise phenotyping. Classical functional supplementation allowed the identification of at least eight genetic groups for MHV, with most of the complementary groups located to the replica’s gene. The creation of selective recombination has allowed more developed and comprehensive studies of the accessory and structural genes of MHV, transmissible gastroenteritis virus (TGEV), and feline infectious peritonitis virus (FIPV), taking advantage of the naturally high levels of homologous RNA-RNA recombination and host range determinants in the S protein. Research with natural variants and controlled genetic recombination experiments have shown that the S protein is the main determinant of host selection, tropism, and pathogenesis; other genetic elements,
likely in the replicase, may affect these characteristics of various coronaviruses. The capacity of coronaviruses to alter host distribution, dissemination, pathogenesis, and disease was developed in the laboratory utilizing cell adaptation and virus passage and was demonstrated in nature by natural variants of MHV, TGEV, and bovine coronavirus (B-CoV), as well as experiments utilizing heterologous viruses such as canine coronavirus (C-cov) to vaccinate cats against FIPV. Besides, selective recombination experiments have established the genetic resilience of the coronavirus genome and the capacity of coronaviruses to restore wild type replication after deletions, mutations, replacements, and rearrangements of gene order in the structural and accessory genes. Challenges for genetic studies utilizing natural variants and mutants have hindered advancement in genetic studies, especially in identifying the specific modifications that are responsible for altered phenotypes [16,17]. Targeted recombination, though a versatile method with efficient filtering, has been restricted to studies of the MHV genome's 310 kb, and is limited to choosing viable recombinants.

**Viral replication complex formation and function**

Replication complexes are sites for the translation of the replicase gene and polyprotein replicase, as well as for the production of viral RNA. Replicase protein genes are known to mediate positive-strand, negative-strand, sub-genomic, and genomic RNA synthesis, as well as capping, polyadenylation, RNA unwinding, viral RNA synthesis template flipping, and discontinuous transcription and transcription attenuation. The coronavirus replicase polyproteins and mature replicase proteins constitute the largest and most complex range of any family of positive-strand RNA viruses recognized and expected distinct enzymatic functions [18,19]. Until recently only the proteinase, RNA helicase, and RNA-dependent polymerase activities were expected or experimentally verified of the 15 or more mature replicase proteins. With the advent of SARS, broader bioinformatics analyzes also culminated in forecasts of many specific RNA processing functions including methyltransferase and exonuclease activities. But with the addition of remote expected associations, no projected or verified roles remain for up to eight of the replicase proteins [20].

**Expression of structural and accessory genes**

Only the most replicase gene in 5 is interpreted from the positive-strand genome RNA data. The genome contains multiple other genes for the known structural proteins S, E, M, and N, as well as other protein expression genes that have been labeled as "non-structural" or "accessory" because they are presumed not to be required for replication and are not considered to be incorporated into virions [21]. MHV codes six of these genes, while SCoV probably encodes up to 11 structural and accessory genes derived from sub-genomic mRNAs. Sub-genomic RNA transcription happens during minus RNA synthesis by acquiring the anti-leader RNA sequences from the 5 end of the genome through homology to a transcriptional regulatory sequence (TRS, also known as an intergenic sequence) and allowing a discontinuous operation of the nascent minus-strand template and polymerase complex in order to acquire the chief [22]. The consequence of transcription is the production of a "nested group" of sub-genomic negative-strand RNAs all comprising the anti-leader sequences that act as models for sub-genomic mRNAs of similar duration. This transcriptional technique shows numerous genes such as the 5 ORF in separate mRNAs, both of which often include the downstream 3 portion of the gene, including the un-translated 3 area of the genome [23].

**Clinical features**

COVID-19's clinical characteristics range from asymptomatic to severe respiratory distress syndrome, including multi-organ failure. Fever (not in all), cough, sore throat, fever, exhaustion, anxiety, myalgia, and breathlessness are typical health characteristics. Conjunctivitis was identified, too. They are also distinct from other respiratory pathogens. In a subset of patients the disease may progress to pneumonia, respiratory failure, and death by the end of the first week. This development is related to severe changes in inflammatory cytokines like IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNFα [17]. The mean time from symptom initiation to dyspnea was 5 days, hospitalization 7 days, and acute respiratory distress (ARDS) syndrome 8 day. In the reported sequence, the need for intensive care treatment was present in 25-30 percent of impacted patients. Witnessed injuries involved severe damage to the heart, ARDS, trauma, and acute kidney damage. Recovery starts in week 2nd or 3rd. Of those who survived the mean period of hospital stay was 10 days. Adverse effects and mortality are more frequent in elderly people and others with existing comorbidities (50 75 percent of fatal cases). The fatality incidence ranged from 4 to 11 percent of injured adult patients. It is calculated that the average case fatality rate ranges between 2 and 3 percent [1].

**Diagnosis**

A suspicious case is characterized as one with fever, sore throat, and cough that has travel history to China or other areas of frequent local spread or interaction with patients with similar travel background, or those with reported COVID-19 infection. Cases can however be asymptomatic or sometimes without fever. Basic treatment of respiratory samples (nasopharyngeal swab/spitum and bronchoalveolar lavage) is based on clear molecular studies. Viruses may also be found in the urine, and blood in extreme situations. It is worth noting that the commercially usable multiplex PCR panels do not contain the COVID-19. For a suspicious case for India, the correct sample needs to be submitted to approve test laboratories in India or the National Institute of Virology in Pune. If the disease advances, clinical testing may become available. Many research examinations are usually non-specific [24].

**Differential diagnosis**

The differential classification covers all forms of respiratory viral infections [influenza, parainfluenza, RSV, adenovirus, human metapneumovirus, non-COVID-19 coronavirus], atypical species (Mycoplasma, Chlamydia), and bacterial infections. COVID-19 can-
not be scientifically isolated from such pathogens or by regular laboratory research. While the past of travel becomes significant. The travel past would thus become meaningless as the disease spreads [25].

**Diagnostic criteria**

The viral research institution in China has carried out a tentative discovery of the SARS-CoV-2 via the postulates of the classical Koch and description of its morphology by electron microscopy. To date, COVID-19's golden therapeutic diagnostic tool is nucleic acid identification by real-time PCR in the screening of nasal and throat swab or other respiratory tract samples and further verified by next-generation sequencing.

**Treatment**

The first move is to maintain sufficient separation to prevent exposure to other partners, patients, and health-care staff. Mild disease can be treated at home with advice on symptoms of risk. The normal values are hydration and diet management, and fever, and cough regulation. For reported cases the daily usage of antibiotics and antivirals like oseltamivir can be prevented. In hypoxic patients it is suggested that oxygen is given by nasal prongs, face mask, high flow nasal cannula (HFNC), or non-invasive ventilation [26]. Mechanical ventilation and also help with extra body membrane oxygen can be required. For others, replacement renal therapy may be needed.

Antibiotics and antimicrobials are required where infections are reported or confirmed. The position of corticosteroids is unproven; although the latest international opinion and the World Health Organization advise against their usage, Chinese recommendations suggest short-term corticosteroid therapy in COVID-19 ARDS [27,28]. WHO has released comprehensive recommendations for critical care management for COVID-19 [25]. As of now, there is no licensed treatment for COVID-19. Based on the experience of SARS and MERS, antiviral drugs including ribavirin, lopinavir-ritonavir has been used. In recent research on the regulation of SARS patients, patients diagnosed with lopinavir-ritonavir with ribavirin had improved results when opposed to those given ribavirin alone [19]. In the case sequence of 99 hospitalized patients with COVID-19 infections from Wuhan, oxygen was provided to 76%, non-invasive ventilation to 13%, mechanical ventilation to 4%, extracorporeal membrane oxygenation (ECMO) to 3%, continuous renal replacement therapy (CRRT) to 9%, antibiotics to 71%, antifungals to 15%, glucocorticoids to 19% 75 percent of the patients were given antiviral medication consisting of oseltamivir, ganciclovir, and lopinavir-ritonavir.

Many medicines recommended for diagnosis include arbidol (an antiviral medication used in Russia and China), intravenous immunoglobulin, interferons, chloroquine, and COVID-19 retrieved plasma. Recommendations on the usage of conventional Chinese herbs can also be included in the Chinese guidelines [29].

**Prevention**

Although no therapies for this infection are approved at this time, avoidance is key. Non-specific features of the disease, infectivity well before the initiation of signs during the incubation phase, dissemination from asymptomatic individuals, lengthy incubation time, tropism for mucous surfaces such as the conjunctive, extended length of the disease and spread even after surgical recovery render it impossible to deter this infection. It is recommended that you isolate confirmed or suspected cases of mild disease at home. Indoor ventilation will be perfect with sunlight to enable virus destruction. Patients should be asked to wear a simple surgical mask and do hygiene for cough. Once in the same space as the patient, nurses will be told to wear a surgical mask and to use hand washing every 15-20 min.

In COVID-19 the biggest danger is transmission to healthcare staff. 21 per cent of those impacted were healthcare staff in the 2002 SARS outbreak [30]. Nearly 1500 healthcare staff in China has been contaminated with six deaths so far. The doctor who originally warned about the virus has also died. Protecting healthcare workers is critical for maintaining quality of treatment and avoiding spread of infection to other patients. Although COVID-19 transmits as a droplet pathogen and is classified by the China National Health Commission in Category B of infectious agents (highly pathogenic H5N1 and SARS), the infection management steps suggested are those for category and agents (cholera, plague).

**Practice point from an Indian perspective**

The coronavirus incidence in India at the time of writing this article is extremely small. Yet the next few weeks can alter that. Hence the advice is as follows:

- Medical professionals will take travel records with any individuals with respiratory problems, including all overseas travel during the previous 2 weeks, as well as interaction with globally travelled ill persons.
- They can set up an outpatient hospital triage program for patients with respiratory disorder, and supply them with a clear surgical mask to use. We also will use surgical masks while treating these patients and regularly exercise hand grooming.
- Suspicious cases should be sent to insolation centers and testing centers approved by the government (at this time Kasturba hospital is located in Mumbai). Consumer research kits are also not eligible in India [31].
- Patients admitted with severe pneumonia and acute respiratory distress syndrome should be evaluated and placed under contact and droplet isolation for travel history. Standard surface decontamination is necessary. If logistics enable, and if no
pathogen is detected, refer the samples for SARS-CoV-2 processing, they should be screened for etiologies using multiplex PCR panels.  

• All clinicians should keep up to date on recent developments including global disease spread.  
• At this time, non-essential international journeys should be avoided.  
• Citizens should avoid sharing rumors and misleading facts regarding the epidemic, and try to reduce general fear and anxiety.

CASE STUDY

A 61-year-old lady has attended our hospital for 4 days moaning of myalgia and febrile feeling. She had interaction with her daughter eight days before her admission to our hospital, which was confirmed 2 days before the hospital visit to be COVID-19-positive. Since therapy with leflunomide (20 mg daily), hydroxychloroquine (200 mg daily), methylprednisolone (2 mg daily), meloxicam (7.5 mg daily), famotidine (20 mg daily), and folic acid (1 mg daily), the woman was diagnosed with RA in a nearby clinic 3 years earlier. The individual had rejected the practice of smoking and consuming alcohol. The nurse showed no clinical problems after admission and her vital signs were as follows: blood pressure, 169/79 mmHg; pulse rate, 80 beats/min; body temperature, 37.6°C; and breathing rate, 20 breaths/min. No pharyngeal injection and strong lung noises have been detected after clinical inspection. The original clinical testing showed that there were no suspicious results on the full blood count, liver function indicators, and C-reactive protein level within the usual range in a chest X-ray. Blood analysis and examinations were both negative for Streptococcus pneumoniae, Mycoplasma pneumonia, Chlamydia pneumonia, Legionella pneumophila, and Mycobacterium tuberculosis. The patient experienced dry cough, scanty sputum, and sore throat three days after admission, with no serious respiratory signs, such as shortness of breath or chest pain. The amounts of C-reactive protein were significantly elevated and chest X-ray revealed haziness in the lower right lung region, indicating COVID-19 pneumonia. The patient was treated with lopinavir/ritonavir for 10 days; 2 tablets (Lopinavir 200 mg/Ritonavir 50 mg) were administered twice daily. Leflunomide and methylprednisolone were removed from the RA medications; but the individual proceeded to obtain hydroxychloroquine, meloxicam, and famotidine. Her condition slowly changed during the antiviral medication, and 10 days during admission her C-reactive protein rates returned to normal. Twenty-four days after admission, PCR was unable to identify SARS-CoV-2 nucleic acid in real-time, so the patient was discharged without any complications.

DISCUSSION AND CONCLUSION

COVID-19 triggered by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China in December 2019 and has spread quickly across the world contributing to the coronavirus pandemic in 2019-2020. COVID-19 frequency ranges greatly, from asymptomatic to severe respiratory distress syndrome. Most reports of COVID-19 include patients aged 30-80. The COVID-19 epidemic rapidly swept through China and spread to 85 countries/territories/areas beyond China as of 5 March 2020. Scientists have made strides in characterizing the novel coronavirus, and they work widely on the virus treatments and vaccinations. This new outbreak of the virus has challenged China's cultural, medical, and public health infrastructure and its neighbours to some extent, particularly to other countries. Time alone can say how this virus affects our lives here in India. Mortality in healthy persons is small, and patients with COVID-19 have only mild symptoms and recover without any special treatment. Around 19% of patients experience extreme pneumonia, with a mortality risk of 2%. Elderly patients with pre-existing comorbid conditions such as heart disease, diabetes, chronic respiratory disease, or cancer are at high risk. Nevertheless, it is uncertain how serious COVID-19 is in Rheumatoid arthritis patients undergoing immunosuppressant.

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